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Original Research Article

A comparative study of serum electrolytes, calcium and phosphorus levels in end stage renal disease patients undergoing hemodialysis

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ABSTRACT

End stage Renal Disease (ESRD) represents the terminal stage of Chronic Kidney Disease (CKD) stage 5 where in there is accumulation of toxins, fluid and electrolytes which are normally excreted by the kidneys resulting in the uremic syndrome which leads to death unless the toxins are removed by renal replacement therapy, using dialysis or kidney transplantation.

Aims & Objectives: To estimate and compare the serum levels of electrolytes, calcium and phosphorus in ESRD patients before and after hemodialysis sessions.

Materials and Methods: Cross sectional study conducted on 70 ESRD diagnosed patients, aged 30-75years of either gender on maintenance Hemodialysis. Blood samples were collected before and after Hemodialysis, analysed for Serum Electrolytes by semi autoanalyser from Roche. Serum Calcium and Phosphorus using Cobas Integra 400 plus from Roche for which Internal and External Quality Assurance Programmes are maintained. The data obtained was analysed using statistical package SPSS 20 version. The parameters are compared using paired 't' test, the test of probability less than 0.05 ($P < 0.05$) considered as statistically significant.

Result: There is significant decrease in mean serum Potassium, Chloride and Phosphorus, significant increase in serum Calcium and no change in serum Sodium after hemodialysis.

Conclusion: Thus from our study we conclude that monitoring serum electrolytes, calcium and phosphorus have prognostic significance in ESRD patients undergoing hemodialysis.

1. Introduction

CKD is an International public health problem affecting 5–10% of the total population.[1] Global Burden of Disease 2015 study estimated that 1.2 million people died from kidney failure. In addition, the estimated number of disability-adjusted life years (DALYS) attributable to kidney disease globally increased from 19 million in 1990 to 33 million in 2013.[2] In India, the approximate prevalence of CKD is 800 per million population, and the incidence of ESRD is 150-200 per million population.[3]

CKD is defined as kidney damage or GFR < 60 ml/min/1.73m^2 for 3 months or more irrespective of cause.[4] Unfortunately CKD is "under- diagnosed" and "under-treated" resulting in lost opportunities for prevention. ESRD represents the terminal stage of CKD (stage 5) where the accumulation of toxins, fluid and electrolytes normally excreted by the kidneys results in the uremic syndrome which leads to death unless the toxins are removed by renal replacement therapy, using dialysis or kidney transplantation.[5]

As the kidney function declines, there is a progressive deterioration in electrolytes and mineral homeostasis with alteration in serum concentrations of the same. Derangements of mineral metabolism occur in patients with ESRD, disturbances of which if not diagnosed and treated will lead to progressive decline in renal functions & cause cardiovascular changes and have a greater impact on patient's well-being leading to increased morbidity and

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mortality.

Hemodialysis has made survival possible for more than a million people throughout the world who have ESRD with limited or no kidney function. Dialysis is defined as the diffusion of molecules in solution across a semipermeable membrane along an electrochemical concentration gradient.[6] The primary goal of hemodialysis is to restore the intracellular and extracellular fluid environment that is characteristic of normal kidney function.[7]

Sodium is the chief cation of the extracellular fluid which is required for the maintenance of osmotic pressure and fluid balance. Potassium is the major intracellular cation which maintains intracellular osmotic pressure. Hyperkalemia is common in ESRD patients due to progression of reduced urinary output, reduced potassium clearance, shift of potassium from the intracellular to the extracellular space in renal failure, which predisposes to cardiovascular disturbances and sudden death and post hemodialysis serum potassium decrement have an arrhythmogenic effect. Estimation of serum sodium and potassium is of importance in cases of renal failure because kidney regulates and maintains a narrow range of electrolyte fluctuation.[8]

Disturbances of bone and mineral metabolism are common. Sudden change of serum calcium levels are associated with arrythmias. Hyperphosphatemia has emerged as an important clinical issue in dialysis patients over the past decade because higher levels of serum phosphate and calcium-phosphorus (Ca x P) product have now been associated with increased vascular calcification and cardiovascular mortality.[9] Hyperphosphatemia leads to increase risk of cardiovascular morbidity and mortality. In this background study is taken up to evaluate the pre and post dialysis electrolyte, calcium and Phosphorus changes in ESRD patients undergoing hemodialysis.

2. Materials and Methods

A cross sectional study was conducted on 70 patients aged 30-75years of either gender who were diagnosed with ESRD (CKD stage 5), undergoing maintenance hemodialysis, willing to give written informed consent were included in the study. The study was carried out for a period of 18 months from January 2019 to June 2020.

Information of the patients with ESRD (CKD stage 5) such as history, clinical findings, reports of routine blood investigations, ultrasonography findings was obtained from the clinical case files.

CKD patients are classified into 5 stages based on estimated Glomerular Filtration Rate (eGFR) suggested by Cockcroft-Gault equation and Modification of Diet in Renal Disease Study (MDRD). Stage 5 CKD having GFR< 15ml/min/1.73m^2 undergoing hemodialysis are the ESRD patients included in the study. Mean duration of dialysis was 3.5 – 4 hours.

2.1. Sample size

In a study conducted by Sreenivasulu U et al, referring the Mean Standard Deviation values of Chloride (pre-hemodialysis:102.2±2.29 and post-hemodialysis:101.3±1.92) considering 80% power of study and 5% level of significance, the minimum sample size estimated is 45, considering 5% attrition rate, it is concurred to study a minimum of 48 cases, in our study a total of 70 cases are included.

2.2. Exclusion criteria

1. Patients with acute kidney injury, chronic liver disease, Ischaemic heart disease.
2. Patients with intercurrent illness requiring hospitalization.
3. Patients with Gout, Hyperparathyroidism, Hypoparathyroidism.
4. Immunocompromised patients.

2.3. Methodology

After taking informed consent, under aseptic precautions 5ml of venous blood sample was drawn, one before dialysis and another after dialysis, transferred to plain sterile vacutainer tubes, blood was allowed to clot at 37^{0}C, and then centrifuged at 3000rpm for 10minutes to separate the serum, the sera thus separated was transferred to plain bullet vials and analysed for serum electrolytes, Calcium and Phosphorus in the Clinical Biochemistry Laboratory of ESICMC & PGIMSR, Rajajinagar, Bangalore -10.

Serum Electrolytes was estimated by Direct Ion Selective Electrodes using Semi automated AVL 9180 Electrolyte analyser from Roche Diagnostics.

Reference range

Serum Sodium: 136 -145 mEq/L

Serum Potassium: 3.5 - 5.1 mEq/L

Serum Chloride: 97 -114 mEq/L

Serum Calcium (reference range: 8.6 – 10.2 mg/dl) and Phosphorus (reference range: 2.7 – 4.5 mg/dl) estimated by OCPC and Phosphomolybdate method respectively using fully automated Cobas Integra 400 plus from Roche Diagnostics for which Internal and External Quality Assurance Programmes are maintained.

2.4. Statistical analysis

The measured parameters are expressed in mean and standard deviation. Statistics like mean, standard deviation, minimum value and maximum values are calculated for the parameters. The parameters are compared using paired‘t’ test, the test of probability less than 0.05 ($P < 0.05$) considered as statistically significant. The data analysed using statistical package SPSS 20 version. Data at the beginning of haemodialysis were grouped under pre-HD,

and the data at the end of haemodialysis under post-HD.

3. Results

3.1. Socio demographic features

In our study a total of 70 patients were included based on the inclusion and exclusion criteria, in those 55 (79%) males and 15 (21%) females with minimum age of 36 years, maximum age of 70 years with mean age group of 52.43±8.23 When the subjects were grouped, we found 2 (3%) of patients have diabetes with CKD, 28 (40%) have hypertension with CKD and 38(54%) have both the co- morbidities with CKD and 2(3%) have other causes with CKD. There is increase in percentage of patients with hypertensive and diabetic nephropathy.

Seventy adult patients diagnosed with ESRD on maintenance haemodialysis consisting of 55 men and 15 women with a mean age of 52.4+/- 8.2(range 36 to 70) with minimum age of 36 years and maximum age of 70 years were studied.

There is a decrease in mean Potassium from 5.1± 0.9 to 3.3 ± 0.8 (p< 0.0001), Chloride from 104.3 ± 4.2 to 102.4 ± 4.518 (p<0.0001) after dialysis. There is no change in Sodium from 137.4 ± 4.2 to 137.4 ± 3.9 (p=0.934) after dialysis. Decrease in mean Phosphorus (4.99 ± 1.4 to 2.99 ± 1.03 (p<0.0001)) and Increase in Calcium (8.2 ± 0.8 to 9.2 ± 0.72 (p< 0.0001)) after dialysis is observed. Statistically significant effect of Hemodialysis on serum electrolytes, calcium and phosphorus is seen as shown in Table 1.

The maximum, minimum and mean concentration of Calcium before hemodialysis is 10mg/dl, 5.60mg/dl, 8.17mg/dl and after hemodialysis is 10.50mg/dl, 7.50mg/dl and 9.24mg/dl respectively. The maximum, minimum and mean concentration of Phosphorus before hemodialysis is 9.10mg/dl, 2.70mg/dl and 4.99mg/dl and after hemodialysis is 5.80mg/dl, 1.20mg/dl and 2.99mg/dl respectively. The maximum, minimum and mean concentration of Sodium before hemodialysis is 149.0 meq/L, 128.0 meq/L, 137.39meq/L and after hemodialysis is 144.0 meq/L, 129.0meq/L and 137.43meq/L respectively. The maximum, minimum and mean concentration of Potassium before hemodialysis is 7.0 meq/L, 3.10 meq/L, 5.13 meq/L and after hemodialysis is 4.80meq/L, 1.80meq/L and 3.33 meq/L respectively. The maximum, minimum and mean concentration of Chloride before hemodialysis is 113.0meq/L, 95.0meq/L, 104.26meq/L and after hemodialysis is 114.0 meq/L, 90.0 meq/L and 102.36meq/L respectively as shown in Table 2.

The mean concentration of serum Calcium before and after hemodialysis is 8.2mg/dl and 9.2mg/dl respectively with mean difference of -1.07, which is highly significant (p value <0.0001), the mean concentration of Serum Phosphorus before and after hemodialysis is 4.99mg/dl and 2.99mg/dl respectively with mean difference of 2.00, which is highly significant (p value <0.0001), the mean concentration of serum Sodium before and after hemodialysis is 137.4 mEq/L and 137.4 mEq/L respectively with mean difference of -0.04, which is not significant (p value = 0.934), the mean concentration of serum Potassium before and after hemodialysis is 5.1 mEq/L and 3.3 mEq/L respectively with mean difference of 1.80, which is highly significant (p value <0.0001), the mean concentration of Serum Chloride before and after hemodialysis is 104.3 mEq/L and 102.4 mEq/L respectively, mean difference of 1.90, which is highly significant (p value <0.0001) as shown in Table 3.

4. Discussion

ESRD is a worldwide health problem and is the leading cause of morbidity and mortality in the developing world. Patients with CKD are at high risk for cardiovascular disease (CVD).[10] Hemodialysis is the first line of treatment in almost all patients with ESRD which would postpone renal transplantation. Adequate dialysis has prolonged the survival of patients with improved quality of life.[11] In our study we assessed the pre and post dialytic changes in serum electrolytes, Calcium and Phosphorus in ESRD patients.

In our study among the strong ions, both K^+ and Cl^-exhibited statistically significant decreases during dialysis, whereas Na+ did not change. Present study results showed no change in serum sodium post dialytically 137.4 ± 4.2 to 137.4 ± 3.9 which is consistent with the Barry Kirschbaum et al. study. In chronic Hemodialysis patients, sodium (Na+) balance largely depends on inter dialytic dietary salt intake and intra dialytic Na+ removal. Dialysis patients appear to have a unique set point for serum sodium.

ESRD patients usually presents with hyperkalemia which predispose to cardiovascular effects like decrease in the action potential, widening of QRS complex and prolongation of PR interval.[12–16] ECG changes occurs during haemodialysis due to quick shift of serum K+ which leads to hypokalemia[17] which requires careful monitoring and intervention. Hyperkalemia reduces the resting membrane potential, slows the conduction velocity and increases the rate of repolarization. Hypokalemia on the other hand increases the resting membrane potential, and refractory period, which are potentially arrhythmogenic[18] which is found to be the most frequent cause of mortality in majority of patients on maintenance hemodialysis.

In our study serum potassium was significantly decreased in post-hemodialysis states compared with pre-hemodialysis levels i.e from 5.1± 0.9 to 3.3 ± 0.8 which is consistent with that reported by Abdul-Majeed H et al,[19] Nauman Tarief et al,[12] Barry Kirschbaum,[20] Seethalakshmi C et al,[21] Dr.U.Sreenivasulu et al.[5] where in hyperkalemia persists pre dialytically which turns normal after dialysis. The removal of potassium by haemodialysis is largely determined by the potassium concentration gradient

Table 1: Shows the comparison between pre and post hemodialysis values of serum electrolytes, calcium, Phosphorus and the paired t test analysis values

Biochemical Parameters	Before Hemodialysis Mean±SD	After Hemodialysis Mean±SD	p value
Sodium	137.4 ± 4.2	137.4 ± 3.9	0.934
Potassium	5.1± 0.9	3.3 ± 0.8	<0.0001
Chloride	104.3 ± 4.2	102.4 ± 4.5	<0.0001
Calcium	8.2 ± 0.8	9.2 ± 0.72	<0.0001
Phosphorus	4.99 ± 1.4	2.99 ± 1.03	<0.0001

Table 2: Comparison of serum calcium, phosphorus, sodium, potassium, chloride during before and after hemodialysis sessions in study population

Parameters	Hemodialysis	Mean	Std. Deviation	Minimum	Maximum
Calcium	Before	8.17	0.80	5.60	10.00
	After	9.24	0.72	7.50	10.50
Phosphorus	Before	4.99	1.36	2.70	9.10
	After	2.99	1.03	1.20	5.80
Sodium	Before	137.39	4.15	128.00	149.00
	After	137.43	3.92	129.00	144.00
Potassium	Before	5.13	0.88	3.10	7.00
	After	3.33	0.77	1.80	4.80
Chloride	Before	104.26	4.23	95.00	113.00
	After	102.36	4.45	90.00	114.00

Table 3: Comparison of concentrations of serum calcium, phosphorus, sodium, potassium, chloride before and after hemodialysis in the study population

Parameters	Hemodialysis		Mean difference	Paired t Test		Significance
	Before	After		t Value	P Value	
Calcium	8.2 ± 0.8	9.2 ± 0.72	-1.07	-10.8	0.000	HS
Phosphorus	4.99 ± 1.4	2.99 ± 1.03	2.00	13.8	0.000	HS
Sodium	137.4 ± 4.2	137.4 ± 3.9	-0.04	-0.1	0.934	NS
Potassium	5.1± 0.9	3.3 ± 0.8	1.80	17.3	0.000	HS
Chloride	104.3 ± 4.2	102.4 ± 4.5	1.90	3.7	0.000	HS

HS=Highly Significant, NS=Not Significant

between the plasma and the dialysate, also on the duration, type of dialyzer and blood flow. All these changes are the signs of membrane instability and cardiac arrest or ventricular fibrillation may follow and it has been shown that most of these sudden deaths do not occur during the dialysis session but in the following hours, thus this situation usually requires careful and prompt monitoring.

In our study mean serum chloride level in post-HD patients was low compared to pre HD patients. There is statistically significant reduction in chloride levels from 104.3 ± 4.2 to 102.4 ± 4.5 post dialysis which is consistent with study conducted by Dr. U. Sreenivasulu et al which showed mean serum chloride post - hemodialysis patients (101.3±1.92) were lower when compared to pre-hemodialysis patients (102.2±2.29) and also consistent with the study by Kirschbaum B[20] which showed that mean serum chloride level in post HD patients was low compared to pre-hemodialysis patients.

In the present study we observed that there is a significant increase in serum calcium from 8.2 ± 0.8 to 9.2 ± 0.72 ($p<0.001$) and a reduction in serum Phosphorus levels from 4.99 ± 1.4 to 2.99 ± 1.03 ($p<0.0001$) after dialysis which is consistent with the study conducted by Mohammed Jumaah IA on 55 patients with chronic renal failure undergoing hemodialysis, investigated for serum Calcium and Phosphorus before and after hemodialysis sessions and concluded that the serum Phosphorus showed significant decrease in post hemodialysis compared to pre-hemodialysis while there was significant increase in the serum Calcium in post-hemodialysis compared to pre-hemodialysis which is consistent with the study conducted by Meenakshi GG[22] in 2015 on effect of dialysis on certain biochemical parameters in chronic renal failure patients and they found serum calcium levels in pre-dialysis group were lower and post dialysis group were higher, serum phosphorus levels in pre-dialysis group were significantly higher in comparison with the post- dialysis group.

5. Conclusion

The aim of the study was to estimate and compare serum levels of electrolytes, calcium and phosphorus before and after dialysis in ESRD patients undergoing Hemodialysis.

In the present study we found statistically significant decrease in serum levels of Potassium, Chloride and Phosphorus, increase in serum levels of Calcium and no change in serum Sodium level post hemodialysis. Serum Potassium decrease < 3.5mmol/L (less than the normal potassium range) would cause arrythmias.

As the kidney disease progresses there is increase in phosphorus levels and slight fall in calcium levels. This derangement in mineral metabolism not only leads to skeletal calcification but also calcification in extra skeletal tissue like vascular tissue. Identification of patients on dialysis with extreme values of serum Calcium, serum Phosphorus may be useful in triggering important clinical interventions

Post-dialysis serum concentration of calcium depends upon the dialysate composition of the calcium and also serum available for ultra-filtration. Monitoring and correcting serum electrolyte, calcium, phosphorus abnormalities have prognostic significance in ESRD patients on Hemodialysis. Therefore, electrolytes, calcium, phosphorus values and dialysate fluid should be considered before dialysis for all patients. It is recommended that the dialysate to be altered in accordance with pre dialytic changes for each and every patient to prevent or treat serious effects due to serum electrolyte, calcium and phosphorus imbalance.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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